IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
SMITH et al.
Serial No. 09/662,462
Filed: September 15, 2000
For: NUCLEIC ACID PROBES AND METHODS FOR DETECTING CLINICALLY IMPORTANT FUNGAL PATHOGENS

Atty. Ref.: 2551-49
Group: 1655
Examiner: Goldberg

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February 26, 2000

Assistant Commissioner for Patents
Washington, DC 20231

ALTERNATE RULE 181 PETITION

Sir:

In the event the Examiner refuses the request to withdraw the restriction requirement contained in the attached Response, consideration of the present Alternate Rule 181 Petition, and grant of the same, are requested.

Consideration of the present Alternate Petition is only required in the event the Examiner refused the request to withdraw the restriction requirement of January 25, 2001, for the reasons requested in the attached Response. The attached Response therefore is a request for reconsideration, as required by Rule 181. No fee is believe required for consideration of the present Alternate Petition as consideration of the same is only required in the event the Examiner errs and refuses the withdraw the restriction requirement. Consideration of the present paper is only required therefore because of Patent Office error. Should the Office believe however that a fee is required, the Commissioner is authorized by the attached cover sheet to charge the undersigned's Deposit Account for any required fee. Notice to the undersigned firm of any charge to the Deposit Account however is requested along with an explanation of the charge.

The present Alternate Petition is only required in the event the request to withdraw the restriction requirement of January 25, 2001, as contained in the attached Response is denied. In

the event the present Alternate Petition is considered, the Commissioner is requested to invoke his supervisory authority, pursuant to Rule 181, and have the restriction requirement of January 25, 2001, withdrawn, for the following reasons.

The Examiner required a restriction of the claims of the above into thirteen (13) allegedly separately patentable Groups (i.e., Groups I-XIII). The Examiner indicated however that the subject matter of each of the Groups is classified in Class 435, Subclass 6. In so classifying the subject matter of the claimed invention, the applicants respectfully submit that the Examiner has indicated the subject matter of the claims has not obtained recognition in the art as being directed to subject matter requiring separate inventive effort. Search of all the claimed subject matter would not therefore be an undue burden on the Examiner.

The restriction requirement should be withdrawn as all of the claimed subject matter has been classified in Class 435, Subclass 6, indicating the subject matter of the Examiner's allegedly separately patentable Groups are, in fact, recognized as not requiring a separate field of search. That is, while the Examiner may show claims are distinct based on a separate classification (i.e., thus showing distinct subject matter has obtained recognition in the art is a separate subject for inventive effort and that a separate field of search is required (MPEP §808.02)) the converse should also be true. The Examiner's indication that there is only one Group of distinct subject matter based on a separate classification is evidence that there is, in fact, one distinct invention which is being claimed.

In addition, the Commissioner is urged to appreciate that if the applicants are required to divide the subject matter in to 13 "inventions", as required by the Examiner, the applicants rights to the inventive concept of this application, i.e. the simultaneous detection and identification of the different fungal species in one single assay, may be diminished. The presently claimed

invention is directed, in part, to the use of a specific set of primers and probes. The applicants respectfully submit that the fungi *Aspergillus, Candida* and *Cryptococcus* are responsible for deep mycoses and pose tremendous challenges for clinicians. Moreover, methods for simultaneous detection and differentiation of a wide variety of fungal species with clinical importance have, prior to the present invention, not been described.

The Examiner's requirement for restriction inappropriately divides the subject matter, to the potential detriment of any clinical and/or commercial advantage and applicability of the current invention.

Moreover, the applicants submit it is illogical to divide the invention corresponding to detection methods applicable for the 7 different *Candida* species. *Candida* infections, indicated by the term 'candidoses', are one of the most common invasive fungal infections. It has been recognized that different *Candida* species and subspecies differ in their ability to cause disease, so it should be of clinical importance to identify and type *Candida* isolates. Efficient treatment regimens of fungal diseases require a correct identification of the fungus at the species level.

Thus the grouping of the methods related to detection of the different *Candida* species enables the detection and differentiation of closely related organisms belonging to the same genus in one single assay. With the use of a "fungal universal primer pair" it is possible to amplify the ITS region of most, if not all, fungal species. In addition, all probes are designed such that they are functional under identical hybridization conditions, thus allowing any possible combination.

Similar arguments apply for the *Aspergillus* species, but moreover, it is of particular interest to further combine the groups relating to resp. different *Candida* species and *Aspergillus* species, as described by the Examiner (Groups I-XI). There is a clear link between the two

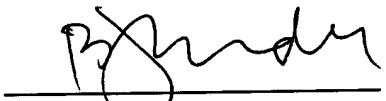
organisms/diseases since candidiasis and aspergillosis account for between 80% and 90% of systemic fungal infections in immuno-comprised patients. In patients with positive fungus cultures, *Aspergillus* species are the second most common isolate after *Candida* species. Since these fungi are most common in deep mycoses it should be important to have detection methods which make it possible to identify the different species. It is known that efficient treatment regimens of fungal diseases require a correct identification of the fungus at the species level.

Based on the above considerations, the applicants submit that, the restriction requirement should be withdrawn.

Withdrawal of the restriction requirement and an early and favorable Action on the merits of all the claimed subject matter are requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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